REMARKS

Applicants appreciate the examination of the present application as evidenced by the final Office Action dated April 15, 2009 (hereinafter, the "Final Action"). Applicants further appreciate the opportunity afforded to inventor, Barry J. Maurer, M.D., Ph.D. and Applicants' representative, Shawna Cannon Lemon, Ph.D., to participate in an interview at the United States Patent and Trademark Office (hereinafter, "USPTO") on June 16, 2009. The substance of this interview is discussed in greater detail in the section below titled "Interview Summary."

At least in view of the claim amendments and remarks presented herein, Applicants respectfully submit that claims 2-9, 13, 15-22 and newly added claim 23 are patentable.

I. Interview Summary

Applicants received an Office communication from the USPTO providing an Interview Summary of the interview conducted at the USPTO on June 16, 2009 (hereinafter, "the interview") with participants Examiner Blessing M. Fubara, Examiner Nelson Blakely, III (observing), inventor, Barry J. Maurer, M.D., Ph.D., and Applicants' representative, Shawna Cannon Lemon, Ph.D. In general, Applicants agree with the substance of the interview as described in the Office communication noting that exhibits and demonstrations were presented during the interview and further noting that Applicants presented evidence to indicate that "the invention administers a flowable powder comprising retinide that when administered as an edible product produces higher plasma levels of the retinide that is more effective in treating proliferative disorders than the capsules of Gibbs or the retinide in the wax of Yessair." Claim amendments were also discussed, and Applicants have amended claim 15 and added new claim 23 in view thereof.

II. Doubling Patenting

Applicants acknowledge that the Examiner has maintained the nonstatutory obviousness-type double patenting rejection. Applicants will provide a terminal disclaimer, if still deemed necessary, upon the indication of allowable subject matter.

III. Claim Rejections Under 35 U.S.C. § 103

Claims 2-9, 13 and 15-22 remain rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,352,844 to Maurer et al. (hereinafter, "Maurer et al.") in view of U.S. Patent No. 4,874,796 to Yesair (hereinafter, "Yesair I") or U.S. Patent No. 5,972,911 to Yesair (hereinafter, "Yesair II") and further in view of U.S. Patent No. 4,665,098 to Gibbs et al. (hereinafter,"Gibbs et al.") and U.S. Patent No. 4,327,116 to Weith (hereinafter, "Weith"). *See* Final Action, page 4. In particular, the Examiner states the following:

> [T]aking the teaching of the prior art, one having ordinary skill in the art at the time of the invention was made would have reasonable expectation of success that modifying the composition of Maurer by using the carrier of Yesair I or II, and delivering the formulation as food item as suggested by Gibbs, the food item having been thickened by flour, would be easily administered to any patient including geriatric or pediatric patient.

Final Action, page 6.

Applicants respectfully traversed this rejection during the interview through demonstration and exhibition as noted above. Applicants reiterate the remarks presented during the interview and submit a Declaration Under 37 C.F.R. §1.132 of Barry J. Maurer, M.D., Ph.D. (hereinafter, "the Maurer Declaration") to further support the pending claims.

As presented to the Examiner and further supported by the Maurer Declaration, the Yesair LYM-X-Sorb (LXS) lipid matrix composition is a solid, bitter-tasting wax at room temperature that rendered clinical patient compliance in the ingestion of a fenretinide/LXS matrix wax quite difficult.

As shown to the Examiner, Gibbs presents fenretinide crystalline powder in a corn oil-containing capsule. This formulation is distinct from the dry flowable powder of the present invention. Moreover, the daily intake of several Gibbs capsules obtained only 1 – 3 micromolar blood plasma levels. Many more capsules (up to 40 capsules per meter-squared of body surface area were needed to obtain 7 – 10 micromolar plasma levels as noted during the interview and discussed in greater detail in the Maurer Declaration.

In contrast, the present inventors found that fenretinide/LXS oral powder obtained

much higher plasma and tissue levels than did the Gibbs formulation at equivalent doses. Further, the sugar-flour powder composition obtained higher drug levels in plasma and brain than did fenretinide in an LXS matrix that had not been so powderized (for example, the wax-based Yesair formulation). *See* the Maurer Declaration for supporting data.

Additionally, during a Phase I clinical trial in pediatric neuroblastoma in 32 patients, the present inventors found that fenretinide/LXS oral powder had high patient compliance with taking the drug and obtained higher plasma drug levels than previously obtained using the Gibbs capsule formulation at equivalent doses. Further, above doses of 774 $mg/m^2/day$, 4 of 18 patients achieved Complete Responses in their tumors (no evidence of tumor), 2 patients of which are still tumor-free at +18 months. Previous studies with the Gibbs capsules produced only one such response in 54 patients. These results, as further discussed in the Maurer Declaration, demonstrate the clear superiority of fenretinide/LXS oral powder over previous oral fenretinide formulations, including the Gibbs formulation.

At least in view of the foregoing along with the Maurer Declaration, it is clear that one having ordinary skill in the art at the time of the invention would not have a reasonable expectation of success of modifying the cited references to achieve the present invention. Moreover, even if combined, the references would not provide the **dry flowable powder** composition given the distinct physical properties of the Yesair composition and the Gibbs formulation and the failure of Weith to supply the missing disclosure.

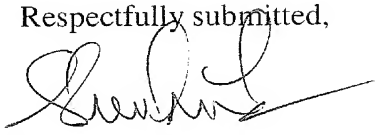
In an effort to further highlight the distinctions, Applicants have amended claim 15 to recite that the edible composition for delivery of a retinide comprises a dry flowable powder and that the **dry flowable powder** comprises the components recited therein. Thus, the composition is not a wax (Yesair I or II) or a crystalline powder in a corn-oil medium (Gibbs). Claim 23 further recites that the retinide is a ceramide-generating retinoid or a retinoic acid derivative. Support for this new claim can be found in the specification as originally filed, for example, at page 5, lines 24-25.

At least in view of the foregoing, Applicants respectfully submit that claims 2-9, 13 and 15-23 are patentable over the cited references, and Applicants respectfully request that the claim rejections under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Accordingly, Applicants respectfully submit that the present application is in condition for allowance and the same is earnestly solicited. The Examiner is encouraged to telephone the undersigned at 919-854-1400 for resolution of any outstanding issues.

Respectfully submitted,



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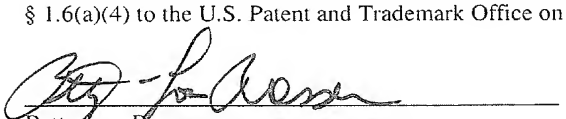

Betty Lou Rosser
Date: August 13, 2009